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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/218,277 | 12/22/98 | EISENBACH-SCHWARTZ M | EISHENBACH=3 |

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| EXAMINER | |
|---|---|
| TURNER, S | |
| **ART UNIT** | **PAPER NUMBER** |
| 1647 | 19 |

**DATE MAILED:** 07/27/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/218,277 | Elsenbach-Schwartz |
| **Examiner** | **Art Unit** |
| Sharon L. Turner, Ph.D. | 1647 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 3-5-01

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 3-7, 9-13, and 16-19 is/are pending in the applica

4a) Of the above, claim(s) 9-13 and 17-19 as set forth herein is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 3-7, 9, 10, 13, 16, 17, and 19 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 3-7, 9-13, and 16-19 are subject to restriction and/or election requirem

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

**Supplemental Response to Amendment**

1. This office action is supplemental to the previous office action mailed 5-17-01.

2. The amendment filed 3-5-01 has been entered into the record and has been fully considered.

3. Claims 3-7, 9-13 and 16-19 are pending.

4. Applicant's continued traversal of the Restriction requirement set forth in Paper No. 13, mailed 8-15-00 appears moot as the restriction requirement was made final in Paper No. 15, mailed 12-15-00. If applicant wishes to pursue the matter further they should file a petition in accordance with 37 CFR 1.144.

However, to further clarify the record applicants response 3-5-01 directs that the examiner has maintained the restriction in that the claims of Group I and Group II achieve different effects as claimed, may be differently classified and require different searches. Applicants continued traversal states that the examiner is incorrect in stating that the two groups as claimed in claim 16 are separable in that they achieve different effects as claimed. This argument is based on applicant's rewording of claim 16 such that the methods of Group I and Group II are now recited together in a single claim. Applicants further contend that as claim 16 is a valid generic claim, both groups and all species must be examined once the generic claim is found allowable.

In response the examiner notes that applicants newly presented claim 16 in fact recites the method of Group I and Group II in a single claim. However such recitation does not negate the

fact that the claim is separable as defined in the restriction of 8-15-00. The different methods achieve different effects, may be differently classified and require different search and examination considerations. A reference for one would not necessarily be a reference for the other. The two methods are drawn to 1) preventing or inhibiting axonal *degeneration* and 2) promoting nerve *regeneration.* The methods are separable as evidenced by the following literature references which establish a separate status in the art of *axonal regeneration* and *axonal degeneration* which are diametrically opposed processes and are patentably distinct as evidenced by Plata-Salaman et al., (1991) Peptides 12(3):653-63, George et al., (1995) J. of Neuroscience 15(10):6445-52, Petrovich et al., (1997) 19(5):551-4, Bradbury et al., (1998) Eur. J. of Neurosci., 10(10):3058-68, Pan et al., (1997) Neurosci. & Biobehav. Reviews 21(5):603-13 and Wang et al., (2000) J. of Neuropath. & Exp. Neurol., 59(7):599-606. The methods may be separately classified for example in class 435, subclasses 374, 375 or 377. The search and examination of both groups together represents a burden to the examiner, regardless of any similarity in reagents or steps. Thus, it is further noted that as such the claim is not properly generic as the methods do not share the characteristics of a genus, i.e., a common utility or function. Alternatively, the claims define distinct methods with different use, different modes of operation, different function and different effects, see in particular MPEP 803.02 and 806.04. It is also noted that no claim is indicated allowable and thus applicants are not presently entitled to the search and examination of any other group or species of the claimed invention. Again, the requirement is still deemed proper and is therefore made FINAL.

5. Claim 16 to the extent of promoting nerve regeneration and to the extent of (a), (c), (d), (e) and (f), and claims 9-13, and 17-19 to the extent of the nonelected species are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. The elected species is to a method of delivering antigen, specifically Myelin Basic Protein antigen of SEQ ID NO:12. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

6. This application contains claims 9-13 and 16-19 drawn to an invention nonelected with traverse in Paper No. 15. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

***Claim Objections***

7. Claims 3-7, 9-13, and 16-19 are objected to under 37 CFR 1.75(c), as being drawn to nonelected subject matter and thus to multiple, patentably distinct inventions.

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants claim fails to specifically delineate a disease but instead recites exclusions of a disease which is not an autoimmune disease or a neoplasm. The claim further refers to 'said

disease'. The term 'said disease' appears to lack direct antecedent basis as no disease was initially defined, but only excluded. Therefore the metes and bounds of the "said diseases" appears to be indefinite with respect to the metes and bounds of the claims. The definition appears to be only what it is not and does not appear to limit the claim to any particular disease.

***Priority***

10. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Israel on 5-19-98. Applicant has filed a certified copy of the application as required by 35 U.S.C. 119(b), received as Paper No. 18, 5-16-01.

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

12. Claims 3-7, 9-10, 13, 16-17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Ling et al., WO96/16085, 30 May 1996 as evidenced by Yucel et al., J. Of Glaucoma 8:38-45, 1999, Enoch et al., Documenta Ophtalmologica, 50:169-184, 1980, and Poser et al., Clin. Neurol. and Neurosurg., 96:103-110, 1994.

Ling et al., teach example 2 and 9-11 comprising administration of MBP(87-99) a myelin basic protein derivative and epitope to animals suffering from EAE, a model which mimics multiple sclerosis. The administration inherently provides an effective amount as provided in example 2, .1 ml of equal volume of MBP peptide or analogue dissolved in PBS and emulsified in Freund's adjuvant supplemented with 4 mg/ml heat-killed Mycobacterium tuberculosis, H37RA. Co-immunization of the peptide analogue specifically inhibited the induction of EAE a form of neuronal degeneration by MBP 87-99 but did not inhibit induction of EAE by MBP(68-88). Neuronal degeneration was measured by clinical score. Thus, the reference teachings anticipate the claimed invention.

Applicants argue that EAE is not a form of neuronal degeneration and that EAE, like MS involves degeneration of myelin and not degeneration of neurons. Applicants do not understand why the rejection is applied to claims 3 and 4 as the injuries and diseases specified are not EAE or MS. Further applicants state that neurological assessment by clinical score is not a measurement of neuronal degeneration and that the Ling reference does not teach neuronal degeneration anywhere in the disclosure.

Applicant's arguments filed 3-5-01 have been fully considered but are not persuasive. In response to applicants argument that EAE and MS are not forms of neuronal degeneration it is noted that applicants own specification teaches to the contrary, see in particular pps. 1-3, which teach that damage to the nervous system (NS) results from diseases and injuries including multiple sclerosis, and that a consequence of such is the loss of adjacent neurons and neuronal

cell death. Further applicants have provided the reference Hauben et al., J. of Neuroscience, September 1, 2000, 20(17):6421-30 which recognizes EAE and MS as diseases which suffer from neurodegeneration, see in particular abstract which teaches preservation of tissue and neuroprotection in such models. This reference also contradicts applicants assertion that clinical score is not a measurement of neuronal degeneration, see in particular Figure 4, EAE clinical scores as a measure of spinal cord recovery, referred to as a neurological paralysis scale. Moreover, the skilled artisan recognizes the Merck Manual of Diagnosis and Therapy, 1992 including reference to multiple sclerosis pp. 1488-90 and identification of neuronal pathology, symptoms and signs including destroyed axons. It is noted that the claim amendment has now limited "the human" of the claims to "one having said disease (or injury)." Claims 3 and 4, similar to claim 5 are directed to effects of an injury or disease selected form those recited in the group, the elected species being glaucoma and trauma. Thus, it is now a requirement that the diseases or injuries be met by the claim with similar effects, herein argued and amended to degenerative effects which may be indicated for example as clinical score, a measure of neurological paralysis. Such is specifically related as a (neuro)degenerative effect of injury and disease of the central and peripheral nervous system, including of trauma and glaucoma. Evidence for such is included for example in Yucel et al., J. Of Glaucoma 8:38-45, 1999, see in particular abstract which teaches that among optic nerve changes in experimental glaucoma is a decrease in the ratio of myelinated fiber area, consistent with MS disease and neurodegenerative affects. It is also recognized that glaucoma and optic neuropathy are associated with trauma and

multiple sclerosis, see in particular abstract, Enoch et al., Documenta Ophtalmologica, 50:169-184, 1980. With respect to trauma specifically, it is noted that trauma plays a role in the pathogenesis of multiple sclerosis, see in particular Poser et al., Clin. Neurol. and Neurosurg., 96:103-110, 1994. Thus, the reference teachings anticipate the claimed invention as set forth.

13. Claims 3-7, 9-10, 13, 16-17 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Weiner et al., US Patent No. 5,858,364 filed May 31, 1995 and issued Jan. 12, 1999 as evidenced by Yucel et al., J. Of Glaucoma 8:38-45, 1999, Enoch et al., Documenta Ophtalmologica, 50:169-184, 1980, and Poser et al., Clin. Neurol. and Neurosurg., 96:103-110, 1994.

Weiner et al., teach administration of NS-specific antigen myelin basic protein (MBP) an epitope to animals, see in particular Examples 1-5, and MBP epitopes or derivatives, see in particular Example 16. The administrations are effective to ameliorate disease and injury brought about by neuronal degeneration as measured by histologic examination clinical score. The effective amount of MBP differs variably based upon route of administration but include for example oral administration of 500 ug MBP, see in particular, column 12, line 18 and immunization by injection with 50 ug MBP, see in particular, column 12, line 6. Immunogenic epitopes were specifically tested in example 16. Thus, the reference teachings anticipate the claimed invention.

Applicants argue that Weiner, like Ling deals with the treatment of multiple sclerosis and as indicated above MS involves degeneration of myelin and not degeneration of neurons.

Applicants conclude that therefore MS is not a disease in which patients are in need of the prevention or inhibition of axonal degeneration and/or promotion of nerve regeneration.

Applicants arguments filed 3-5-01 have been fully considered but are not persuasive as set forth above. MS patients clearly suffer from neuronal degeneration in addition, if not resulting from degeneration of myelin. Such is supported by applicants specification, applicants submitted post-filing date publication and further by the knowledge of the skilled artisan as recognized by the Merck Manual. It is not necessary that either Ling or Weiner teach "neuronal degeneration" per say. They are only required to teach an effect of neuronal degeneration which is clearly included by the EAE and MS model system as indicated by EAE clinical score, a measure of neurological paralysis. With respect to the recited disease and injury of glaucoma and trauma, Yucel, Enoch and Poser as set forth above teach the prevalence of myelin degeneration and neurodegeneration consistent with trauma and glaucoma. Thus, the reference teachings anticipate the claimed invention.

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 3-7, 9-10, 13, 16-17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ling et al., WO96/16085, 30 May 1996, Weiner et al., US Patent No. 5,858,364 filed May 31, 1995 and issued Jan. 12, 1999, Enoch et al., Documenta Ophtalmologica, 50:169-184, 1980, and Poser et al., Clin. Neurol. and Neurosurg., 96:103-110, 1994.

Ling et al., and Weiner et al., teach the administration of MBP antigens for the treatment of multiple sclerosis as set forth above.

Ling et al., and Weiner et al., do not specifically teach the prevalence of MS in glaucoma or upon traumatic injury.

Enoch et al., and Poser et al., specifically teach the prevalence of neurodegenerative effects and myelin degeneration in multiple sclerosis, glaucoma and among patients with trauma.

Thus, it would have been prima facie obvious to the skilled artisan that the neuroprotective benefits provided to multiple sclerosis patients which exhibit neurodegeneration, myelin degeneration, glaucoma and symptoms resultant from trauma would benefit from the coincident treatment of MS as the diseases and injuries are consecutive. One of skill in the art

would have an expectation of success as the patients of Ling and Weiner are accorded positive effects. The artisan would clearly recognize that the patients and symptomatology merely coincide to each other. Thus, the reference teachings render the claimed invention obvious.

***Status of Claims***

16. No claims are allowed.

***Conclusion***

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts

to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
July 16, 2001

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600